Multimodality evaluation of the viability of stem cells delivered into different zones of myocardial infarction.

Journal: Circ Cardiovasc Imaging

Publication Year: 2008

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PubMed link: 19808509

Funding Grants: In Vivo Molecular Magnetic Resonance Imaging of Human Embryonic Stem Cells in Murine Model of Myocardial Infarction

Public Summary:
This study investigates the role of multiple imaging techniques to assess the location, survival, and effects of stem cells following delivery into 3 different areas of injured mouse heart: normal, near the injury, and inside the injury. Magnetic resonance and bioluminescence imaging were implemented to analyze the stem cells and heart function. The location and survival of the stem cells and their effects on the heart were readily determined. The stem cells delivered into the normal region demonstrated highest survival. However, the stem cells delivered near the injury demonstrated highest improvement in the heart function. This study demonstrates that both the survival and the area of delivery are critical in restoring the injured heart.

Scientific Abstract:
BACKGROUND: We tested the hypothesis that multimodality imaging of mouse embryonic stem cells (mESCs) provides accurate assessment of cellular location, viability, and restorative potential after transplantation into different zones of myocardial infarction. METHODS AND RESULTS: Mice underwent left anterior descending artery ligation followed by transplantation of dual-labeled mESCs with superparamagnetic iron oxide and luciferase via direct injection into 3 different zones of myocardial infarction: intra-infarction, peri-infarction, and normal (remote). One day after transplantation, magnetic resonance imaging enabled assessment of the precise anatomic locations of mESCs. Bioluminescence imaging allowed longitudinal analysis of cell viability through detection of luciferase activity. Subsequent evaluation of myocardial regeneration and functional restoration was performed by echocardiography and pressure-volume loop analysis. Using 16-segment analysis, we demonstrated precise localization of dual-labeled mESCs. A strong correlation between histology and magnetic resonance imaging was established ($r=0.962$, $P=0.002$). Bioluminescent imaging data demonstrated that cell viability in the remote group was significantly higher than in other groups. Echocardiography and pressure-volume loop analysis revealed improved functional restoration in animals treated with mESCs, although myocardial regeneration was not observed. CONCLUSIONS: Multimodality evaluation of mESC engraftment in the heterogeneous tissue of myocardial infarction is possible. Magnetic resonance imaging demonstrated accurate anatomic localization of dual-labeled mESCs. Bioluminescent imaging enabled assessment of variable viability of mESCs transplanted into the infarcted myocardium. Echocardiography and pressure-volume loop analysis validated the restorative potential of mESCs. Although mESCs transplanted into the remote zone demonstrated the highest viability, precise delivery of mESCs into the peri-infarction region might be equally critical in restoring the injured myocardium.